

Characterizing the relationship between sesame, coconut, and nut allergy in children

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Sesame and coconut are emerging food allergens in the United States. We sought to examine whether children allergic to peanuts and tree nuts are at increased risk of having an allergy to sesame or coconut. We performed a retrospective chart review of children who underwent skin prick testing (SPT) to sesame and coconut and identified 191 children who underwent SPT to sesame and 40 to coconut. Sensitization to sesame was more likely in children with positive SPT to peanuts (odds ratio [OR] = 6.7, 95% confidence interval [CI] [2.7–16.8], $p < 0.001$) and tree nuts (OR = 10.5, 95% CI [4.0–27.7], $p < 0.001$). Children with histories of both peanut and tree nut reaction were more likely to have a history of sesame reaction (OR = 10.2, 95% CI [2.7–38.7], $p < 0.001$). Children with sensitization or allergy to peanuts or tree nuts were not more likely to be sensitized or allergic to coconut. In conclusion, children with peanut or tree nut sensitization were more likely to be sensitized to sesame but not coconut. Children with clinical histories of both peanut and tree nut allergy were more likely to be allergic to sesame.

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Pediatric food allergy is increasing in prevalence, and peanuts and tree nuts are among the most common causes of severe allergic reactions (1–3). Children with peanut or tree nut allergies may be at higher risk of developing allergies to previously less well-recognized foods such as sesame (4–6) and coconut (7). With the high prevalence of peanut and tree nut allergy in the United States and concern for potential cross-reactivity with sesame, allergists suggest screening peanut and tree nut allergic children for sesame allergy (8). With the recent consideration of coconut as a tree nut in food labeling practice, some allergists are testing for coconut as well (9).

Sesame is an emerging food allergen in the United States and carries a significant risk of severe reactions including anaphylaxis. In a case series from Israel, 30% of patients with sesame allergy had anaphylaxis as their first presenting symptom and all were <1 yr of age (10). Of significant clinical concern is that sesame allergy can begin in children who are too young to

describe their symptoms and the risk of severe allergic reactions is high (10–12). The prevalence of sesame allergy varies geographically, with increased allergy in regions of greatest exposure. In Israel, where sesame is regularly consumed in the diet, sesame is the third leading cause of food allergy after egg and cow's milk and the second leading cause of anaphylaxis after milk (13). With immigration and globalization, more American children are being exposed to sesame through their diets, making sesame an emerging cause of severe allergy in the United States. In addition to sensitization via direct exposure to sesame, there is hypothesized cross-reactivity between nuts and sesame (14–16).

Coconut is an allergen that is also gaining more notice in the United States. Immediate hypersensitivity to coconut is a relatively new phenomenon, first described in two adult patients with walnut allergy (17). Coconut allergy remains rare, with only a small number of reported cases (7, 17–19). However, there is new interest in this

allergen as coconut is now considered a tree nut for food labeling purposes (9).

There are few studies examining the risk of sesame and coconut sensitization and clinical allergy among nut allergic patients. We sought to determine the prevalence of sesame and coconut sensitization among our population and the risk of sensitization and clinical allergy to sesame and coconut in our nut allergic patients.

Methods

Study design

This study was a retrospective chart review of skin prick test (SPT) results at Children's Hospital Boston and several affiliated outpatient clinics from December 2006 through March 2008. Patients ranged in age from 6.6 months to 19.6 yr (median, 4.0 yr). Subjects underwent SPT to various allergens. All subjects avoided short-acting antihistamines for 72 h and long-acting antihistamines (loratadine, cetirizine, fexofenadine, and hydroxyzine) for 10 days prior to SPT. Standardized extracts were used for testing to peanut, hazelnut, cashew, Brazil nut, almond, walnut, pistachio, pecan, sesame, and coconut. Control tests for SPTs were performed with histamine (positive control) and normal saline (negative control). Wheal diameters were measured at 15 min. A positive SPT was defined as a wheal diameter at least 3 mm larger than the diameter of the negative control.

The study population consisted of all patients who underwent SPT to sesame and all patients who underwent SPT to coconut. Data were also collected on SPT results to peanut and tree nuts, if performed. Tree nuts in our population were defined as hazelnut, cashew, Brazil nut, almond, walnut, pistachio, or pecan. Clinical history of allergic reaction to peanut, tree nuts, sesame, and coconut was collected for all patients. Symptoms of allergic reaction included urticaria, eczema exacerbation, non-specific dermatitis, angioedema, vomiting, diarrhea, repeated coughing or sneezing, wheezing, or anaphylaxis. History of allergic reaction was determined by patient or parent/guardian reporting as documented by the physician in the written medical record.

Statistical analysis

Prevalence rates of sensitization and clinical reaction for each food allergen were calculated. We created 2×2 tables to determine cross-reactivity between two different foods. We calculated odds ratios (OR) and 95% confidence intervals

(CI) from 2×2 tables. ORs indicated the risk of sensitization to one food in the pair if sensitized to the other food in the pair. Statistical significance was assessed by Pearson's chi-square or Fisher's exact method, as appropriate. A p-value of < 0.05 was considered statistically significant.

For sesame and coconut, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of a positive skin test were determined with regard to a history of clinical allergic reaction.

Results

Study population

The study population consisted of all patients who underwent SPT to sesame or coconut ($N = 212$) (Table 1). Several children underwent SPT to both sesame and coconut ($N = 19$). Therefore, of the total study population, 191 children underwent SPT to sesame and 40 to coconut. The prevalence of sesame and coconut sensitization in this pediatric population was 36.6% and 20.0%, respectively.

Sesame and coconut sensitization among peanut and tree nut sensitized children

The proportion of sesame sensitization was 53.3% ($N = 40$) among peanut sensitive children, 57.7% ($N = 41$) among tree nut sensitive children, and 68.9% ($N = 31$) among those sensitized to both peanuts and tree nuts. Sensitization to sesame was more likely in children with positive SPT to peanuts (OR = 6.7, 95% CI [2.7–16.8], $p < 0.001$) and tree nuts (OR = 10.5, 95% CI [4.0–27.7], $p < 0.001$). Further, children sensitized to both peanuts and tree nuts were more likely to be sensitized to sesame (OR = 6.1, 95% CI [2.9–12.6], $p < 0.001$). There was no significant association between sensitization to peanuts or tree nuts and coconut (Table 2).

Table 1. Characteristics of study population

	Sesame		Coconut	
Total patients skin tested	191		40	
Age, median (yrs)	4.0		4.0	
Skin prick test result	Positive	Negative	Positive	Negative
N (%)	70 (36.6)	121 (63.4)	8 (20.0)	32 (80.0)
History of clinical reaction, N (%)	10 (14.3)	13 (10.7)	2 (25.0)	7 (21.9)
Age, median (yrs)	4.8	3.6	4.3	4.0

Table 2. Cross-reactivity among various food allergens based on skin prick testing (SPT). Odds ratio (OR) represents the likelihood of sensitization to the food in the second column if already sensitized to the food(s) listed in the first column

Food allergen cross-reactivity by SPT		OR	95% CI	p value
Peanut	Sesame	6.7	2.7–16.8	<0.001
Tree nut	Sesame	10.5	4.0–27.7	<0.001
Peanut and tree nut	Sesame	6.1	2.9–12.6	<0.001
Peanut	Coconut	4.6	0.4–51.1	0.319
Tree nut	Coconut	1.6	0.1–31.8	1.000
Peanut and tree nut	Coconut	2.1	0.2–27.1	0.498
Sesame	Coconut	1.1	0.1–8.9	1.000

Sesame and coconut allergic reactions among peanut and tree nut allergic children

The proportion of sesame allergy was 13.2% (N = 9) among peanut allergic children, 14.8% (N = 4) among tree nut allergic children, and 50.0% (N = 5) among those allergic to both peanuts and tree nuts. Children were not more likely to have an allergic reaction to sesame if they had a history of allergic reactions to peanuts (OR = 1.4, 95% CI [0.6–3.5], $p = 0.443$) or tree nuts (OR = 2.1, 95% CI [0.6–7.0], $p = 0.207$). However, children with a history of allergic reactions to both peanuts and tree nuts were more likely to have an allergic reaction to sesame (OR = 10.2, 95% CI [2.7–38.7], $p < 0.001$). There was no increased risk of coconut allergic reaction among peanut or tree nut allergic children (Table 3).

Predictive values of skin testing

Among children with a positive SPT to sesame, 14.3% (N = 10) had a clinical history of allergic reaction to sesame. Additionally, among children

Table 3. Cross-reactivity among various food allergens based on clinical history of reaction. Odds ratio (OR) represents the likelihood of clinical reaction to the food in the second column if there is a prior history of allergic reaction to the food(s) listed in the first column

Food allergen cross-reactivity by clinical history		OR	95% CI	p value
Peanut	Sesame	1.4	0.6–3.5	0.443
Tree nut	Sesame	2.1	0.6–7.0	0.207
Peanut and tree nut	Sesame	10.2	2.7–38.7	<0.001
Peanut	Coconut	0.5	0.1–2.5	0.402
Tree nut	Coconut	2.6	0.6–10.5	0.177
Peanut and tree nut	Coconut	N/A*	N/A*	1.000
Sesame	Coconut	0.9	0.1–7.5	0.930

*We were unable to calculate an OR and CI for this group because one value in the 2×2 table was 0. Specifically, there were 0 children with a history of reaction to both peanuts and tree nuts and to coconut.

Table 4. Predictive value of skin prick testing result for clinical history of allergic reaction for various foods

Food allergen	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Sesame	43.5	64.3	14.3	89.3
Coconut	22.2	80.6	25.0	78.1

with a positive SPT to coconut, 25.0% (N = 2) had a history of clinical allergic reaction to coconut (Table 1). Correlation of SPT result and clinical history of allergic reaction demonstrated that sesame SPT had low sensitivity and specificity but high NPV, while coconut had high specificity and NPV (Table 4).

Discussion

The prevalence of peanut and tree nut allergies in American children is increasing (1–3). The emergence of sesame as a cause of allergic reactions and anaphylaxis is becoming increasingly recognized as well. Laboratory data suggest mechanisms for possible allergen cross-reactivity among nuts and sesame and coconuts (14, 16, 20, 21). However, little is known about the risk of clinical allergy to sesame or coconut in nut allergic children. The aim of this study was to determine whether children with allergies to peanuts or tree nuts were at increased risk of having sensitization as well as allergic reactions to sesame or coconut. We addressed this question by examining both SPT data and clinical reaction history. Our study is one of the largest evaluating SPT data and clinical history of allergic reactions. Furthermore, this is the first study evaluating SPT and clinical history of cross-reactivity for coconut in peanut and tree nut allergic children.

We demonstrated that sensitization to sesame is common among children sensitized to peanuts, tree nuts, or both. Children did not appear to be at a higher risk of sensitization to coconut if they were sensitized to peanuts, tree nuts, or both. We then investigated whether these patterns of sensitivities from our SPT data were reflected in the clinical history of allergic reactions. In contrast to our SPT data, children with clinical allergies to peanuts or tree nuts were not more likely to have a reaction to sesame. However, children with a history of clinical reactions to both peanuts and tree nuts were more likely to have allergic reactions to sesame. Consistent with our SPT data, children did not appear to be at a higher risk of reaction to coconut if they had an allergic reaction to peanuts, tree nuts, or both.

There are few published studies examining SPT among patients sensitized to peanuts, tree nuts, and sesame. In a British study, among 55 patients with peanut or tree nut sensitization, 4 (7%) had a positive sesame SPT (4). Our study, performed 15 yr later in an American pediatric population, shows an even higher degree of sesame sensitization. We showed that 53.3% of peanut sensitized children and 57.7% of tree nut sensitized children have a positive SPT to sesame. The prevalence of sesame sensitization may be higher in our study because of the differing ages and geographies of the populations or may be a result of the fact that peanut, tree nut, and sesame allergies have increased over time (8). Another group examined Australian children with peanut allergies and showed there was an increased prevalence of sesame sensitization and allergy in children who remained peanut allergic compared to those who outgrew their peanut allergies (15). Interestingly, this increased prevalence occurred despite strict recommendations to avoid sesame, suggesting a role for possible antigenic cross-reactivity. This study did not examine the relationship between tree nut and sesame allergy. A recent American study showed that the proportion of sesame allergy, defined as a convincing clinical history and evidence of positive sesame-specific IgE, was 6% among peanut allergic children (5). We found a higher proportion of sesame allergy (13.2%) among our peanut allergic patients. These differences are likely reflective of our differing study populations. Further, we reported the proportion of sesame allergy was 14.8% among tree nut allergic patients and 50.0% among children allergic to both peanuts and tree nuts.

Maloney et al. (22) determined the strength of association between various food allergens using serum-specific IgE measurements. By calculating Spearman rank order correlation coefficients, they demonstrated that there was a weak correlation between peanut and sesame (0.34) and only a moderate correlation between certain tree nuts and sesame (range 0.57–0.79). This group did not investigate SPT data, nor did they calculate correlations based on clinical history. Although we did not examine serum-specific IgE levels, these results are consistent with our findings that children with clinical allergies to peanuts or tree nuts are not more likely to be allergic to sesame.

Shared homology between sesame and peanut and tree nut allergens have been described, suggesting a mechanism for cross-reactivity and sensitization (14, 16, 20). Seed storage proteins have been implicated as the major coconut

allergen. Shared homology between the seed storage proteins of coconut and several tree nuts, primarily walnut and hazelnut, has been described (21). However, we found no evidence of increased coconut sensitization or clinical allergy in tree nut allergic patients.

An important limitation of our study is that the diagnoses of food allergies were based on physician documentation of patient or parent/guardian reporting of convincing histories of reactions. For ethical and practical reasons, we did not verify these reports with double-blind placebo-controlled food challenges, which remain the gold standard for diagnosing food allergies. Additionally, the group sizes of patients sensitized or allergic to specific foods, particularly coconut, were relatively small. Larger studies will need to be performed to verify these results. Despite these limitations, this study is important because it evaluates the potential cross-reactivity of several prominent food allergens in a larger patient population and in more detail than published previously.

Our study adds to the small body of literature defining predictive values for sesame SPT (6) and is the first to define predictive values for coconut SPT. In this study, we defined SPT results as either positive or negative and did not further validate these results in double-blind placebo-controlled food challenges for the reasons described earlier. However, we have shown in another patient population that sesame SPT is not a good predictor of true sesame allergy as defined by oral food challenge (23). In that group, although we could not define a diagnostic decision point for sesame SPT, there was a trend for more predictability for SPT compared with sesame-specific IgE and a SPT wheal size of <3 mm approached a NPV of 90%.

In summary, our study shows that both cross-sensitivity and clinical cross-reactivity occur between peanuts and tree nuts with sesame but not coconut. Specifically, children with sensitivity or clinical allergy to both peanuts and tree nuts are significantly more likely to be sensitized or allergic to sesame. This study fails to demonstrate a significant risk of sensitization or allergy to coconut in peanut or tree nut sensitized or allergic children. Our differing results for sesame sensitivity vs. clinical reaction in peanut and tree nut allergic children, coupled with our data demonstrating the low PPV of sesame SPT, brings into question the utility of the current practice among many allergists of screening peanut allergic children for sesame sensitivity. If future studies can show SPT reliably predicts sesame allergy, screening may then be appropri-

ate, especially given the high risk of anaphylaxis among young children on their first exposure to sesame. However, there are risks of diagnosing sesame sensitivity without a history of allergic reactions: (i) the burden of dietary restriction and avoidance measures and (ii) possibly losing the ability to acquire and sustain oral tolerance. For now, we recommend considering evaluating children for sesame allergy if they are allergic to peanuts or tree nuts and have never previously ingested sesame. If sensitization is demonstrated, oral challenge to sesame may be required to document the presence of clinical reactivity before recommendations are made for avoidance. If the child is already eating sesame without reactions, the child is clinically tolerant and further testing is not recommended. There does not appear to be sufficient data at this time to recommend that all peanut and tree nut allergic children undergo testing for coconut allergy. Future studies will be needed to validate our findings in a larger patient population and to further define the predictive values of sesame and coconut SPT against the gold standard of food challenges.

References

- BOULAY A, HOUGHTON J, GANCHEVA V, et al. A Euro-Prevall review of factors affecting incidence of peanut allergy: priorities for research and policy. *Allergy* 2008; 63: 797–809.
- FLEISCHER DM. The natural history of peanut and tree nut allergy. *Curr Allergy Asthma Rep* 2007; 7: 175–81.
- MUNOZ-FURLONG A, WEISS CC. Characteristics of food-allergic patients placing them at risk for a fatal anaphylactic episode. *Curr Allergy Asthma Rep* 2009; 9: 57–63.
- EWAN PW. Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations. *BMJ* 1996; 312: 1074–8.
- GREEN TD, LABELLE VS, STEELE PH, et al. Clinical characteristics of peanut-allergic children: recent changes. *Pediatrics* 2007; 120: 1304–10.
- HO MH, HEINE RG, WONG W, HILL DJ. Diagnostic accuracy of skin prick testing in children with tree nut allergy. *J Allergy Clin Immunol* 2006; 117: 1506–8.
- NGUYEN SA, MORE DR, WHISMAN BA, HAGAN LL. Cross-reactivity between coconut and hazelnut proteins in a patient with coconut anaphylaxis. *Ann Allergy Asthma Immunol* 2004; 92: 281–4.
- BEAUSOLEIL JL, SPERGEL JM. Late diagnosis of tree nut and sesame allergy in patients previously sensitized but tolerant to peanut. *Ann Allergy Asthma Immunol* 2006; 97: 443–5.
- Food Allergen Labeling and Consumer Protection Act of 2004 (Public Law 108-282, Title II). Section 201(qq), added October 2006.
- DALAL I, BINSON I, LEVINE A, SOMEKH E, BALLIN A, REIFEN R. The pattern of sesame sensitivity among infants and children. *Pediatr Allergy Immunol* 2003; 14: 312–6.
- DERBY CJ, GOWLAND MH, HOURIHANE JO. Sesame allergy in Britain: a questionnaire survey of members of the Anaphylaxis Campaign. *Pediatr Allergy Immunol* 2005; 16: 171–5.
- SPORIK R, HILL D. Allergy to peanut, nuts, and sesame seed in Australian children. *BMJ* 1996; 313: 1477–8.
- DALAL I, BINSON I, REIFEN R, et al. Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. *Allergy* 2002; 57: 362–5.
- BEYER K, GRISHINA G, BARDINA L, SAMPSON HA. Identification of 2 new sesame seed allergens: Ses i 6 and Ses i 7. *J Allergy Clin Immunol* 2007; 119: 1554–6.
- HO MH, WONG WH, HEINE RG, HOSKING CS, HILL DJ, ALLEN KJ. Early clinical predictors of remission of peanut allergy in children. *J Allergy Clin Immunol* 2008; 121: 731–6.
- LEDUC V, MONERET-VAUTRIN DA, TZEN JT, MORISSET M, GUERIN L, KANNY G. Identification of oleosins as major allergens in sesame seed allergic patients. *Allergy* 2006; 61: 349–56.
- TEUBER SS, PETERSON WR. Systemic allergic reaction to coconut (*Cocos nucifera*) in 2 subjects with hypersensitivity to tree nut and demonstration of cross-reactivity to legumin-like seed storage proteins: new coconut and walnut food allergens. *J Allergy Clin Immunol* 1999; 103: 1180–5.
- ROSADO A, FERNANDEZ-RIVAS M, GONZALEZ-MANCEBO E, LEON F, CAMPOS C, TEJEDOR MA. Anaphylaxis to coconut. *Allergy* 2002; 57: 182–3.
- TELLA R, GAIG P, LOMBARDERO M, PANIAGUA MJ, GARCIA-ORTEGA P, RICHART C. A case of coconut allergy. *Allergy* 2003; 58: 825–6.
- BEYER K, BARDINA L, GRISHINA G, SAMPSON HA. Identification of sesame seed allergens by 2-dimensional proteomics and Edman sequencing: seed storage proteins as common food allergens. *J Allergy Clin Immunol* 2002; 110: 154–9.
- BENITO C, GONZALEZ-MANCEBO E, DE DURANA MD, TOLON RM, FERNANDEZ-RIVAS M. Identification of a 7S globulin as a novel coconut allergen. *Ann Allergy Asthma Immunol* 2007; 98: 580–4.
- MALONEY JM, RUDENGREN M, AHLSTEDT S, BOCK SA, SAMPSON HA. The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy. *J Allergy Clin Immunol* 2008; 122: 145–51.
- PERMAUL P, STUTIUS LM, SHEEHAN WJ, et al. Sesame allergy: role of specific IgE and skin prick testing in predicting food challenge results. *Allergy Asthma Proc* 2009; 30: 643–8.